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ORIGINAL ARTICLE

A Structured Approach to the Prevention of Psychoactive Substances Use in Vulnerable Populations and the Therapeutic Interventions in the Case of Patients Diagnosed with Substance Use Disorders – A Romanian Society-focused Perspective

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Abstract: The phenomenon of substance use disorders (SUDs) presents extremely complex etiopathogenesis with intermingled psychological, social, economic, and biological factors. Therefore, the prophylactic and therapeutic approach is multidimensional and should involve targeting all the aforementioned variables. However, it is frequently difficult to separate these factors and construct specific strategies to mitigate their direct negative effects, so caution is needed when formulating recommendations for this population, starting from guidelines for case management and finishing with optimization of healthcare policies. Based on the lack of good practices approved at the national level in Romania for the prevention and treatment of SUDs, this article suggests a draft for such an instrument that could help both clinicians and decisional factors with attribution in healthcare and drug abuse prevention. The methods used in this article are (1) a literature review of studies, guidelines, and other reviews focused on specific aspects of drug abuse/dependence and (2) expert opinions derived from clinical and administrative experience. The results are formulated as recommendations, scored according to the GRADE system, and grouped into three categories: (1) preventative measures for SUDs, (2) secondary prophylaxis, (3) therapeutic and other SUD-targeted interventions. In conclusion, the need for guidelines and policies focused on the prevention and treatment of SUDs, especially in vulnerable populations, is an unmet need in our country. The suggested algorithm in this paper tried to bridge the gap between the available literature dedicated to SUDs, practical experience, and future policies in the healthcare of patients with SUDs.

Keywords: substance use disorders, withdrawal, detoxification, post-detoxification, harm reduction, opioid agonists, opioid antagonists, disulfiram, acamprosate

INTRODUCTION

European Union Drugs Agency (EUDA) is the main EU institution with responsibilities in the domains of monitoring the regional drugs of abuse (DOAs) and formulating evidence-based practice guidelines, and its most recent published report, in 2024, showed the following data with epidemiological, social, and clinical implications: cannabis is the most commonly used illicit drug in Europe (approximately 8% in European adults used cannabis during the last year, and 1.3% are estimated to be daily or almost daily users of cannabis); cocaine is the second most frequently used illicit drug in Europe, but the prevalence and use patterns considerably vary across countries (2.5% of European adults used cocaine in the last year, and this drug is responsible for an important percentage of the deaths related to drugs use); synthetic stimulants (including synthetic cathinones), MDMA (ecstasy), heroin and other opioids, and new psychoactive substances (NPAs) are other important threats to the health of adult population (but also tending to incorporate younger adults and adolescents); although less known to the large public, hallucinogens, anaesthetics, dissociative and sedative agents are also use illicitly in EU (for example, lysergic acid diethyamide – LSD, ketamine, gamma hydroxybutyrate – GHB, nitrous oxide, or hallucinogenic mushrooms) and able to raise multiple difficulties both individual- and social-grounded [1].

The latest European Drug Report regarding drug-induced deaths, an indicator that refers to the total cases of drug overdose deaths, showed an increase in this indicator in the year 2022 in some EU countries, with a provisional estimate of 6400 drug-induced deaths [2]. Opioids, frequently in combination with other substances,

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remain the most reported cause of drug-induced deaths, and heroin was involved in approximately 1800 deaths in the EU [2]. However, synthetic opioids, e.g., fentanyl derivative carfentanil and nitazene opioids, are increasingly represented in these statistics [2]. Although a significant number of these deaths are accidental, in other cases, the intent (or lack of it) is difficult to ascertain; therefore, particularities among the EU countries regarding the methodology of evaluation of overdose intentionality should be noted when comparing the results. For example, in Hungary, Netherlands, Slovenia, and Sweden, more than 30% of the overdose deaths among women were considered triggered by suicidal intent, while in Bulgaria, Poland, and Finland, suicidal intent was recorded for over 25% of deaths among women in the year 2022 [2].

The threats related to substance use disorders (SUDs) in younger populations have been described worldwide. In the US, according to multiple reports, more than 40 million people aged 12 and older received a diagnosis of SUD in 2020, and the Center for Disease Control and Prevention (CDC) signaled overdose deaths in children aged 10 to 19 more than doubled from 2019 to 2021 [3]. Adolescents are especially vulnerable to the negative impact of SUDs in the long term at multiple levels, involving mental health problems, sub-standard academic performance, and family, social, and physical health complications [4]. For example, psychotic-like experiences are more frequent in young substance users than in non-users, and this may indicate a subclinical at-risk population for psychosis [5-8].

Special attention is needed in the post-COVID-19 pandemic era regarding the challenges related to patients with SUDs, especially because this population is considered more vulnerable to infections and somatic complications or comorbidities, and many countries still have outbreaks of this viral disease [9-12]. Therefore, this vulnerability should be considered when planning large-scale interventions or designing policies for patients with SUDs, and distinct resources should be allocated due to the risk of problematic evolution in those individuals with dual diagnoses.

According to the data presented in the Romanian "National Drug Strategy 2022-2026" [13], the three substances that produce the highest rates of requests for medical assistance in our country are (1) cannabis, (2) opioids, and (3) NPAs. The same document shows that the main aspects that require intensive monitoring in Romania are: (1) special care for populations at increased risk of addiction, mainly high school students, due to their high consumption of cannabis and NPAs; (2) infectious diseases associated with drug use, especially HIV, and type B and C hepatitis viruses, in medical personnel taking care of individuals who inject themselves DOAs; (3) the rate of deaths associated with drug use is on an increasing trend, against the background of methadone intoxications; (4) problematic use of opioids at the national level, with heroin being the main drug of consumption; (5) drugs use during incarceration -mainly opioids, but also cannabis and NPAs- a phenomenon that steady increased from 2013 to 2019; (6) drug crime and related problems, diversion of drug precursors (designer-precursors) and drug market dynamics (decreasing price of cocaine and increasing purity of the product, as well as increasing the availability for most types of DOAs) [13].

From the perspective of vulnerabilities, the same document mentions (1) economic aspects - shortage of specialized human resources, de-professionalization, underfunding, persistent dysfunctions in the organization of public service systems (health, education, social assistance), accentuated by the COVID-19 pandemic; (2) legislative and organizational aspects - collection of data on drugs, integrated assistance for these patients, monitoring of drug precursor operations; (3) aspects related to the international drug market - high availability at European level of synthetic and natural drugs, the emergence of new synthetic opioid substances, increased consumption of MDMA and cannabis, and the emergence of new cannabis derivatives; (4) access of organized crime groups to emerging technologies that increase the efficiency of their actions, a fact translated in the volume of drug trade that significantly increased [13].

The general objectives of the national drug strategy 2022-2026 are (1) strengthening the national prevention system, addressed to the general population, schoolchildren and vulnerable groups; (2) developing services and interventions within the national medical, psychological and social assistance system aimed at reducing the negative effects associated with drug use; (3) strengthening and developing specialized medical, psychological and social reintegration interventions and services; (4) developing an integrated approach to drug use in penitenciaries; (5) strengthening interventions to fight against organized crime entities with activities in the field of drug trafficking; (6) strengthening the capacity to detect large quantities of drugs, precursors and pre-precursors; (7) strengthening the mechanism for controlling the illicit circuit of precursors and narcotic drugs and fighting drug production; (8) intensifying the effective monitoring of the logistical and digital channels used for drug distribution and the confiscation of illicit substances; (9) international cooperation to reduce the demand for and supply of DOAs; (10) developing and strengthening an integrated system for collecting data on the drug abuse phenomenon; (11) ensuring a unified framework for action in the field of drugs and precursors, monitoring the implementation of national drug policies, efficient use of resources and maximizing the results of the interventions carried out [13].

Considering all the previously presented data regarding the main directions of the DOAs' risk analysis, the necessity of preventing these drugs' use at the national level, and the objective of approaching therapeutically vulnerable populations, this paper aims to formulate recommendations targeting these essential aspects.

MATERIALS AND METHODS

Based on the existing data in the literature and the experts' opinions, directions of action for the core domains of DOA use prevention and treatment of patients diagnosed with SUDs are presented and grouped into distinct categories. The recommendations are hierarchized using a methodology based on the GRADE system (Grading the Recommendations Assessment, Development, and

Evaluation), which allows the scoring of strengths from very low (D) to low (C), moderate (B), and high (A) [14-16]. Each of the authors scored the strength of the recommendations in the first round of evaluation, while in the second, a consensus was searched. In cases where a consensus cannot be reached, the recommendation will include a comment referring to the disagreement and its reason.

RESULTS

All the recommendations have been distributed according to their main theme in (1) directions for the prevention of DOAs; (2) the role and directions of secondary prophylaxis; (3) educational and therapeutic interventions for SUDs.

According to the International Classification of Diseases, 11th edition [17], Table 1 represents the main classes of DOAs. The recommendations (and the literature reviews on which they are based) refer mainly to alcohol, cannabis and its synthetic derivatives, opioids, sedatives, and related drugs, cocaine and other psychostimulants, synthetic cathinone, hallucinogens, nicotine, and volatile inhalants.

Literature review and summary of recommendations

1. Directions for the prevention of the use of DOAs

Multiple-component programs have been associated with positive results because they incorporate school, family, and community resources and can be integrated into a psychoeducational framework, which is more effective than just delineating „forbidden" or „dangerous" zones from the „allowed" ones [18]. On the other hand, information in itself did not lead to sustained change, although some effects were observed regarding the modification of knowledge and attitudes [18]. Skills training-based programs are also useful [18]. According to the US National Institute of Drug Abuse [19] principles for prevention, the main directions that should be at the foundation of any guidelines dedicated to this objective include enhancing protective factors and neutralizing the risk factors; the interventions must be tailored to the target population; such interventions have to be long-term and repeated, in order to reinforce the original objectives [19]. Regarding alcohol abuse, the most effective prophylactic measures can be considered those limiting the availability of alcohol, establishing a minimum age for drinking, restrictions on hours and days of the sale, and different availability of alcohol-strength- drinks; regulations on drinking and driving also have been proved efficient; early treatment interventions, rules of promotion in mass media, as well as education and persuasion in schools and universities are also associated with favorable results [18]. Integrated policies for alcohol abuse prevention have been the most consistent interventions associated with good outcomes [18].

Table 1: Classification of the drugs of abuse according to the ICD-11 [17]

Alcohol
Cannabis
Synthetic cannabinoids
Opioids
Sedatives, hypnotics and anxiolytics
Cocaine
Stimulants (incl. amphetamines, methamphetamines, methcathinone)
Synthetic cathinones
Caffeine
Hallucinogens
Nicotine
Volatile inhalants
MDMA (3,4-methylenedioxymethamphetamine) or related drugs, including MDA (3,4-Methylendioxyamphetamine)
Dissociative drugs, including ketamine and phencyclidine (PCP)
Other specified psychoactive substances, including medications

Prevention of SUDs among adolescents according to the United Nations Office on Drugs and Crime (UNODC) World Health Organization (WHO) Informal Scientific Network should respect several recommendations, between them being promoting population-based and environmental prevention measures; enhancing the meaningful engagement of vulnerable groups in prevention initiatives and fighting stigmatization; deployment of effective, evidence-based methods in different settings and implementing these interventions along a continuum of care that includes screening, but also brief interventions and treatments (i.e., family therapy, contingency management, and cognitive behavioral therapies-CBT) [20].

The main barriers identified in delivering prevention-focused interventions are unstable funding, lack of coordination between systems, lack of workforce capacity, insufficient knowledge about evidence-based programs, and lack of information about how to adapt programs for certain settings [21,22]. A review that included 30 studies dedicated to the prevention and treatment of opioid

use disorder (OUD) showed that stigma, limited access to treatment, inadequate healthcare infrastructure, regulatory barriers, and lack of clearly focused policies are the main challenges in adequately preventing and treating such disorders; several recommendations, formulated based on the available data are the development of culturally adapted prevention programs, assessment of the long-term effectiveness of potential treatment modalities, encouraging interventions focused on decreasing stigma and improving access to care by using the technology [23].

Socioecological strategies have been explored in the prevention of SUDs by focusing on the interaction between individual, interpersonal, and macro-level, i.e., community, social, and political factors, in the modeling of health outcomes and overall well-being [24]. A public health approach is encouraged when policy, research, and service delivery solutions targeting SUDs are considered [17]. Health equity is essential when applying the framework of socioecology to the prevention of SUDs; although this model is explored by the author of the cited report in the context of the US society, the core principles may be applied irrespective of the social context [24]. For example, public funds for the treatment of overdoses should cover individual, interpersonal, and macro-level investments in the primary, secondary, and tertiary prevention spectrum [24].

Prevention strategies targeting social risk factors modeled for children and adolescents can improve the outcome and decrease the risk of SUD onset [25]. Also, the treatment of SUDs is recommended to correspond to the „Chronic Care Model," with (a) adjustment of the intensity of intervention to the severity of the disorder and (b) the concomitant treatment of psychiatric and organic comorbidities [25]. Between the social risk factors that should be targeted by preventative interventions are, according to epidemiological studies, high intensity of stressors, poor social support, accessibility of drugs, and lack of opportunities for non-drug use behaviors; adverse social environmental exposures increase the risk for SUDs especially when appear in childhood and adolescence due to their impact on the brain development [25].

The National Institute for Health and Care Excellence (NICE) from the UK formulates the following recommendations for delivering drug misuse prevention activities to high-risk individuals for SUDs: health services- primary care services, community-based health services, mental health services, sexual and reproductive health services, drug and alcohol services, and school nursing and health visiting services; specialist services; community-based criminal justice services; accident and emergency services [26]. The initial discussion with the individuals at risk includes a complete assessment of physical and mental health, personal, social, educational and employment circumstances, and any drug use; based on this first assessment, the immediate safety of the person is to be considered [26]. Skills training for children and adolescents who are vulnerable to drug misuse is an important step, highlighted by the NICE guidelines, and this type of training has to help them develop listening, conflict resolution abilities, refusal, decision-making, identification and management of stressors, coping with criticism, dealing with a feeling of exclusion, and making healthy behavior choices [26]. Also, the families and important caregivers need to receive skills training, targeting communication, developing and maintaining healthy relationships, conflict resolution, and problem-solving [26]. In the case of the adult population, which is vulnerable to drug abuse, information about the risks of using such drugs should be offered, and also information about the local services where advice and support can be found; campaigns of providing information about drug use should be initiated in settings like nightclubs or festivals, gyms (for individuals who might abuse of steroids, for example), hostels, etc. [26].

Other authors mention the potential usefulness in children and adolescents of anti-substance use messaging, routine screening, clear pathways for referral to treatment in all at-risk settings, and mentoring programs [27]. Involvement of pediatric primary care is considered the most important step due to the possibility of incorporating preventive counseling and screening for substance use [27,28].

Based on the presented data and the particularities of the SUDs in our country, the following recommendations have been formulated:

1.1. Psychoeducational interventions need to target groups at high risk for abuse/harmful use/dependence/SUDs and should be tailored especially for children of school age, adolescents, patients with mental disorders, patients with somatic diseases requiring analgesic treatments, and persons deprived of liberty.

In order to implement a national prevention policy, the participation of the following categories of professionals is required:

a. representatives of primary health care services (GPs);

b. school psychologists and university campus-based psychologists;

c. psychiatrists and psychologists from the National Penitentiary Administration network;

d. psychiatrists and clinical psychologists from the national hospital network;

e. physicians with different specialties who prescribe drugs with abuse potential - oncologists, rheumatologists, specialists in palliative medicine, etc.

Also, integrating family members and other important caregivers in the preventative efforts could be of significant benefit.

The methodology of these interventions includes:

a. training programs for doctors in the primary healthcare network to recognize the specific symptoms of the use of DOAs, under the coordination of specialists trained through the programs mentioned in paragraph 3.1;

b. periodically organized workshops to update the scientific, legal, and practical knowledge of all physicians who approach high-risk

population groups;

c. informative sessions and skills training programs for psychologists working in schools or other educational institutions;

d. educational sessions for educators, teachers, and professors;

e. organizing information groups for families of patients with SUDs or who have risk factors for developing a SUD;

f. establishing a hotline (phone and internet) for first aid dedicated to vulnerable individuals and their relatives;

g. informative leaflets and brochures that family doctors, school psychologists, and teachers may distribute to vulnerable populations.

Monitoring the implementation of these measures and determining their medico-social impact involves an integrated data processing system that can be accessed by all interested parties in order to maintain constant feedback between specialists in different cities and authorized trainers.

2. Secondary prophylaxis of individuals in the recovery phase after SUDs

This type of intervention is focused on early identification of an SUD, followed by approaches that tend to reduce/stop its progression [24]. Screening and referring patients to mental health specialists who can prescribe medications for addictive disorders is a crucial component of this stage of intervention [24]. An analysis of the risks vs. protective factors is also a part of secondary prevention because it can lead to further elaboration of local and national strategies. For example, lack of affordable or accessible treatment services, stigma against people with SUDs, lack of provider knowledge about this pathology, punitive drug policies, and high threshold treatment policies are risk factors approachable by secondary-stage interventions, while receipt of early diagnosis and referral to treatment, stable housing, economic stability, peer recovery support, and availability of quality treatment are protective factors [24]. Interventions used in this stage that were associated with good results in young people diagnosed with SUDs are, based on a systematic review, behavior therapy, Minnesota 12-step programs, residential care, and general drug treatment [29]. Also, involving parents and other significant caregivers may enhance the efficacy of these interventions [29,30]. Multiple levels for these interventions should be provided: college, family, community, peer-led, workplace-based, and technology-driven approaches must be planned and specific techniques must be chosen for each individual [29,30].

Community-based programs have been indicated by several authors as presenting the highest effectiveness if applied in the context of the general population but also in high-risk groups [31]. However, there is great heterogeneity in the interventions and techniques of secondary prevention [31]. Environmental methods have a positive trend because they take into account patients' needs in their natural environment, but cognitive-behavioral methods may also be recommended for this vulnerable population [31]. Experiential interventions in combination with cognitive-behavioral therapies may involve not only patients but also family members, teachers, and other community members and bodies [31].

Regarding the factors that contribute to the secondary prevention of SUDs, different aspects have been evoked, with various degrees of approachability, such as self-efficacy, hopefulness, and social support [31]. Skills training programs may still reinforce resilience factors and mitigate risk factors; therefore, such strategies are needed in this population. Primary care physicians may be involved in this type of prevention by applying screening tools, treating comorbidities, addressing patients to specialized counseling when social stressors are identified, early diagnosis or referral, and administration of brief behavioral change counseling [32].

More specialized interventions for patients with a defined SUD, for example, crack (cocaine) abuse/dependence, have been reviewed, and the results regarding their efficacy were mixed [33]. Behavioral and community-based prevention measures have led to heterogeneous results in the short-term and harm-reduction interventions (e.g., safer crack use kit distribution), but it is considered that they had modest efficacy in risk reduction [33]. Psycho-social therapies, including contingency management, showed some positive results but limited short-term efficacy [33]. Pharmacotherapy also did not produce convincing evidence [33]. Therefore, the authors of the respective review concluded that no „golden standard" prevention strategy exists for crack abuse [33].

As it can be inferred from these data, it is extremely difficult to find evidence-based recommendations for specific drugs, except for nicotine, alcohol, and opioid SUD, where multiple guidelines exist [34-36]. For example, when approaching recommendations for alcohol abuse/dependence, NICE guidelines recommend relapse prevention strategies such as psychological interventions (initiated ideally within two weeks after successful alcohol withdrawal for people with moderate or severe alcohol dependence)- cognitive behavioral therapies, behavioral therapies, behavioral couple therapies, social network and environmental based therapies; pharmacological interventions- acamprosate, oral naltrexone or disulfiram [34]. The American Psychiatric Association (APA) recommends, in its own guidelines, the monitoring of biological biomarkers for early identification of alcohol use disorder (AUD), identification and treatment of co-occurring conditions, the formulation of the therapeutic objectives in agreement with the patients, educational measures included in the therapy, initiation of naltrexone or acamprosate for patients with moderate to severe AUD, or disulfiram in those patients who want to achieve abstinence, prefer this drug, or are intolerant to naltrexone/acamprosate, and in those who are capable of understanding the risks of alcohol consumption while taking disulfiram, and have no contraindication to this drug; topiramate/gabapentin may be initiated in certain conditions [35]. Also, the US Department of Veterans Affairs/Department of Defense guidelines support similar recommendations, adding psychosocial interventions, such as group mutual help techniques (e.g., peer linkage, network support, 12-step facilitation) [35].

Regarding nicotine use disorder (NUD), extensive meta-analyses and clinical studies showed that behavioral treatments, relapse

prevention psychotherapy, pharmacologic therapies, motivational enhancement, smoking reduction to quit, brief advice, alternative intervention modalities, self-help, and tailored treatments can be useful in preparing longer-term abstinence [37]. The European Network for Smoking and Tobacco Prevention (ENSP) guidelines highlight the need for persistent and repeated therapeutic interventions, as well as long-term follow-up visits [38]. According to these guidelines, educational measures and several pharmacological agents might be required after relapse, but no effective treatment has yet been identified to treat tobacco dependence in abstinent smokers [38].

In the domain of OUD, the American Society of Addiction Medicine (ASAM) guidelines showed that strategies directed at relapse prevention should be included in any case management plan for patients receiving active opioid treatment or ongoing monitoring of their health status [39]. Methadone should be reinitiated if relapse occurs after methadone discontinuation or when there is a high risk of relapse, and naltrexone can also be recommended as long-term treatment, with the possibility of its discontinuation if the risk of relapse becomes low [39].

Based on the available data and experts' opinion, the following recommendations are formulated:

2.1. Secondary prevention is facilitated by a comprehensive, bio-psycho-social approach to the patient diagnosed with SUD who is recovering and needs to be taken care of by specialized networking involving mental health workers, GPs, social workers, etc.

More specifically, the participants in this activity are psychiatrists, clinical psychologists, psychotherapists, general practitioners and social workers who have completed professional development programs. These specialists will apply the medical and psychological support techniques acquired during the aforementioned training and will collect epidemiological data necessary to estimate the specific needs of patients in all the regions of our country as a preliminary step for an adequate allocation of financial and human resources. The final goal of this approach is to ensure continuity of medical and psychological care after discharge from the hospital of patients treated for disorders related to DOAs.

Methods to efficiently organize specialized assistance services and to achieve their coordination:

a. the formation of a National Coordination Center for Medical Assistance Services for Patients with Substance Use Disorders would be required;

b. This center will ensure the continuity of healthcare services and related services (psychotherapy, clinical psychology) by integrating data from hospitals that admit individuals with SUDs, healthcare centers that provide methadone substitution therapy and polyclinics that keep records of such patients;

c. the necessary steps will be taken to establish post-detox treatment centers for patients who have a documented history of DOAs withdrawal therapy.

This activity will be monitored by analyzing data at the national level regarding the periodic checks of patients discharged with a diagnosis of SUD, such as relapse rate, duration until the first relapse, duration of medical and psychological supervision, the need for pharmacological resources, specialized equipment, and personnel, etc.

2.2. Guidelines for good practices in drug use prevention necessitate a working group that could be created with the participation of practicing physicians and academics who will oversee the drafting of this guide. Once finalized, the guideline will be submitted for approval by the Ministry of Health, in order to implement its recommendations at the national level.

The methodology includes a systematic review of the literature, exploring guidelines developed by EU societies, associations, and foundations, and an integration of epidemiological data at the national level.

Monitoring will be carried out through periodic reassessments of the level of recommendations for each SUD diagnosis, corresponding to epidemiological data at the national level and data from specific research at the international level.

3. Educational and therapeutic interventions focused on SUDs

The importance of specialized training for physicians involved in the assessment and management of SUDs has been acknowledged worldwide, and the lack of an adequately trained workforce remains a challenge in many countries [40,41]. According to a WHO survey on resources for the prevention and treatment of SUDs, which included 162 countries, deficiencies in the training programs for the workforce managing this pathology exist in almost one-third of the countries, and when low-income countries were analyzed separately, the percentage reached 60 [42]. The same survey concluded that counselors and community health workers benefitted from the lowest rate of specialized training (23% and 19%, respectively) [42].

Several key challenges in the training of specialists in addictive disorders are the lack of an agreed training pathway, gaps in addiction training for the main workforce groups, lack of identification of SUDs, development of new therapeutics that signal a rapidly changing therapeutic landscape, new diagnoses like behavioral addictions, and the necessity to create a common framework that fights stigma [43].

The content of the curricula is still a matter of debate, however, with interactive teaching methods and experiential and didactic components being considered the core of such programs [40]. Addiction specialists should be involved in promoting information about SUDs and refining the skills of medical students and residents, but also in enhancing knowledge on SUDs among practicing physicians, starting from primary-level physicians and up to tertiary center doctors [40]. Also, online programs are an option for the

training of physicians due to decreasing time and other expenditures [40]. Attitudinal skills training refers to enhancing communication that should be patient-centered, focused on patient trust and autonomy, and involve empathy, respect, and compassion [44]. An evidence-based program integrating screening, brief intervention, and referral to treatment (SBIRT) has been created for clinicians confronted with challenges specific to SUDs and is considered time-efficient as a first-line intervention [44,45]. Another brief intervention is FRAMES, an acronym indicating feedback, responsibility, advice, menu for change, empathy, and enhancing self-efficacy [46]. Brief interventions are usually the first step, but they are associated with efficacy in reducing substance use and its harmful consequences, and they can be followed by referrals to appropriate treatment services in more complex SUD cases [44-47].

Long-term and multicomponent training of healthcare specialists dedicated to helping patients with SUDs is considered the most effective means to obtain self-efficacy in providers who may initially be reticent or uncomfortable with taking care of this particular population [48-50]. Several steps have been described in this direction, including institutional pairing (experienced team pairs with local leadership), „train the trainer" programs, telemedicine (virtual consultation technology for ensuring the quality of healthcare), booster sessions, and ongoing assessment of treatment delivery [48].

Closer integration of substance use-related services in the general health care system is a priority highlighted by the US Surgeon General in a report named „Facing Addiction in America" (2016) [51]. Such an integration is expected to address health disparities and costs for patients and caregivers and to improve general health outcomes [51]. The use of HealthIT is encouraged in the same report as a means to integrate different care systems better and to increase its collaborative nature but also to extend the workforce, improve care coordination, and reach individuals who are reluctant to participate in traditional treatment settings [51].

Increasing the psychoeducative approaches to the SUD phenomenon and targeting large populations, not only those most vulnerable, is expected to reduce the stigma associated with this pathology. In this direction, lack of knowledge about the causes of SUDs and the available treatments fuels stigmatization, and the patients' perceived disapproval by others contributes to the enhancement of self-stigmatization [48]. Fliers and brochures published by national and international authorities could reduce the phenomena of stigma and self-stigma [48,52].

Evidence-based interventions are grouped into behavioral treatments (mainly cognitive-behavioral therapy, motivational interviewing, and contingency-management approaches), including peer support interventions (also manualized techniques that encourage Alcoholics Anonymous – AA participation), applied in an individual/group format, but also technology-based treatment; pharmacological strategies for detoxification and relapse prevention (greatest efficacy demonstrated for OUD, NUD, and AUD); combined approaches [48]. The accent should be placed on multidisciplinary teams, which include psychiatrists, psychologists, GPs, teams focused on treating comorbid disorders, community-based health workers, and peer and lay counselors [48].

Harm reduction is defined as an attempt to decrease the negative consequences of drug use in patients who still continue to use such substances, and it appeared as a reaction to the excesses of the „zero tolerance approach" [53]. Although harm reduction has proven effective and its acceptance is increasing, the concept in itself is poorly defined [53]. According to a review dedicated to harm reduction for alcohol, tobacco, and illicit drug use (n=650 articles), there is insufficient evidence to support the extensive adoption of this intervention for any DOAs [54], but these results may be related to the low quality of the included studies. According to another systematic review/meta-analysis, the average effect for harm reduction interventions compared to treatment as usual was 0.03 SD (95% CI, -0.08, 0.14), based on the results of nine studies [55]. Still, in specific populations, such as incarcerated individuals, a meta-analysis showed that syringe service provision and opioid agonist treatment are effective in reducing risk behaviors and needle and syringe sharing (n=126 studies) [56]. Yet another systematic review supports the role of harm-reduction techniques, i.e., early screening for problematic alcohol use followed by brief and other interventions in first-contact medical healthcare facilities in reducing AUD onset [57].

Drug decriminalization is considered a variant of harm reduction and it was conceived that a disproportional exacerbation of drug-related harms and imposed short/long-term burdens on an already stigmatized and marginalized population due to the criminalization of drug use is counterproductive to general health [58]. This decriminalization involves policymakers and clear norms of drug prescriptions for pharmacists who must advocate actively for these policies, according to several authors [58].

Regarding the detox (withdrawal) and post-detox interventions for AUD, according to a systematic review (n=49 studies), medical/pharmacological interventions were less likely to demonstrate efficacy when the outcomes were treatment engagement and recovery, and psychological/psychosocial and technological interventions were more likely to be associated with success [59]. When OUD was considered in another review (n=64 articles), medical and combined interventions performed well, as did psychological interventions with one or multiple reinforcement components [60]. The availability of outpatient withdrawal and detox programs is limited when analyzed globally, and limitations are economical, stigma-related, unavailability of specific programs, and co-occurring mental health disorders [61]. As other authors have pointed out, there is a tendency to underutilize medication that can help in relapse prevention as fast as the detox phase has been overcome, which increases not only the risk of relapse but also of somatic or psychiatric complications [61]. Specific protocols for detox exist, depending on the DOAs involved [62-64]. At any rate, it is essential to consider the complexity of treatment in patients undergoing withdrawal but who are already diagnosed with severe somatic disorders, and hospitalization should always be recommended in these cases [65-68]. Also, the presence of psychiatric comorbidities needs further exploration and adequate treatment, concomitantly with the initiation of the withdrawal therapy [69-73].

The transition from detoxification to maintenance treatment is an important step for the insurance of long-term positive outcomes

in patients with SUDs [74-77]. During this transitional phase, various facilitators or inhibitors may appear at the patient level, program level, or system level [74]. Continuity of care after detoxification heavily influences important outcomes like the rate of readmissions [75]. Patients with OUD who choose to be included in aftercare post-detoxification programs have significantly better outcomes when compared to those who do not have formal aftercare, up to nine months of follow-up [76].

Therapeutic communities for addictions are an evolving concept with very diverse theoretical and practical implications [78]. Such communities are a distinct psychosocial approach to the treatment of SUDs that emphasizes the role of the „community as a method", with the accent being placed on self-help and mutual help, social learning and finding the most appropriate motivation for change [78]. A review of therapeutic communities' effectiveness for addictions (n=16 reports) showed that two out of three studies reached significantly better results (substance use and legal outcomes), and five studies detected superior employment and psychological functioning [79].

The use of guidelines for SUDs in clinical practice is a subject of controversy in the literature. Several aspects that explain this controversial nature of the topic refer to the lack of clear, evidence-based recommendations for the choice of a certain pharmacological agent in the treatment of a special addiction, for example, between methadone, buprenorphine and naltrexone in OUD [80]; heterogeneity of the included studies, populations, methods of monitoring and interventions explored; the gap between the research and practice is derived from the fact that an individual with SUD or a family member will most likely not be offered a treatment drawn from the existing list of extensively studied variants [81]; different variables may interfere with the clinical recommendation of a certain therapy, such as costs, local availability, difficulties in its implementation, etc. [81].

3.1. Specialist training in addiction therapy is a prerequisite for any policy regarding this domain since there are no pre-qualified personnel based solely on faculty or college graduation.

The participants in this activity are physicians specialized in virtually any field of Clinical Medicine related to mental health or Psychology professionals who wish to obtain a certificate of complementary studies on the therapy of substance use disorders to assist patients with this pathology but also to continue acting as trainers of specialists in drug addiction therapy.

The proposed method is a complementary study program with a modular format, coordinated by the Ministry of Health in collaboration with the Romanian Academy - Section of Medical Sciences and the Romanian College of Physicians.

The curriculum of this training course will be realized based on the proposals of a working group of practicing doctors (psychiatrists, ICU specialists, toxicologists, clinical pharmacologists, pulmonologists, etc.) and clinical psychologists with experience in drug addiction and academic staff with teaching duties who are part of specialized departments.

The core themes of this complementary study program will be: (1) the neurobiology of substance use disorders, (2) clinical and diagnostic criteria for substance use disorders, (3) comorbidities and complications of substance use disorders, (4) psychopharmacology of substance use disorders, (5) counseling and psychotherapy techniques specific to substance use disorders, (6) case management in substance use disorders, (7) research methodology in substance use disorders, (8) clinical and psychological monitoring in substance use disorders, (9) methods for preventing relapse in substance use disorders.

The monitoring of this activity will be done periodically by representatives of the program coordinating institutions.

3.2. Intensification of harm-reduction interventions is considered an essential component of prevention and educational programs.

This activity involves non-governmental organizations, outreach teams, and interdisciplinary teams, which include volunteers, doctors, nurses, social workers, etc.

The proposed methods are:

a. training of specialists and volunteers in harm-reduction methods by graduates of the drug addiction therapy training program (according to section 3.1)

b. collection of data on the activity of these teams in order to establish the necessary resources

c. periodic supervision of volunteer teams

This activity will be monitored through an integrated system of periodic evaluation of the number of harm-reduction interventions by specialists trained in the courses in section 3.1.

An indirect parameter of monitoring is the number of HIV/HBV/HCV infections in patients using injectable ARVs and hospitalizations for somatic complications. This parameter is important for assessing the resources required and costs associated with outreach interventions.

3.3. Enhancing the healthcare system's capacity for ensuring adequate detox treatment is an objective that could increase the survival rate in the SUD population, as well as the overall health, quality of life, and general functionality.

The participants in this activity are primary care physicians for the purpose of early identification and referral to a specialist of patients with disorders related to the use of DOAs, but also specialist physicians from the national network who can refer patients with these disorders to hospital, or specialist physicians from the hospital network, responsible for the case management of these patients.

The proposed methods for ensuring superior detox therapy results are increasing awareness of the positive consequences of withdrawal therapy in the medium and long term at the level of vulnerable populations, developing/re-evaluating therapeutic guidelines for patients requiring detox therapy, and encouraging participation in continuous improvement programs for physicians providing detox treatment.

Monitoring is done by periodically evaluating the parameters related to the effectiveness of this therapy - the number of readmissions, the duration until the first relapse, the duration of treatment maintenance, etc.

3.4. Post-detox treatment is a complementary and necessary intervention to the previous step, and it must be observed that, in the absence of a clear continuity of care, the risk of relapse or acquiring short-term or long-term complications or comorbidities is very high.

This component involves all institutional bodies involved in the social, psychological, and medical assistance of patients who have undergone detoxification programs.

The proposed methods include the creation of the national center mentioned in section 2.1, capable of ensuring continuity of care and supervision of the patient with substance addiction after discharge from the hospital.

Monitoring treatment and patients' evolution is done by determining the effectiveness of post-detox therapy using specific effectiveness indicators, such as the number of readmissions, duration of treatment, and number of drug-related crimes committed after discharge.

3.5. Reducing patient access to DOAs is an objective with long-term beneficial consequences, which require the active and continuous participation of specialized institutions.

The participants in this section of care are representatives of the Ministry of Health and the National Anti-Drug Agency, but also other agencies with national representation. Accessibility is defined, in this context, as (1) access to illicit sources (an aspect controlled by law enforcement agencies) and (2) access resulting from the overprescription of drugs with abuse potential (by family physicians and specialist doctors).

The main method is to reduce the overprescription of drugs with abuse potential by doctors (benzodiazepines, barbiturates, opioids, methylphenidate, etc.) by the means of implementing real-time monitoring of these drugs' circuit (preventing the issuance of prescriptions for the same substance by several doctors to a single person). The center mentioned in section 2.1. will also have the objective of developing a program that alerts the prescribing doctor if a patient requests the issuance of drugs with abuse risk even though he/she has recently received another identical prescription.

Monitoring of this step involves the periodic assessment of the level of consumption of SPRA (legal and illegal) by specific means.

3.6. Many practitioners have urged the creation of a treatment guide for patients diagnosed with SUDs, yet there is no clear project for editing such an important work.

The participants in drafting this guide will be practicing physicians and academics with experience in drug addiction therapy. Once finalized, the guide can be submitted for approval by the Ministry of Health to implement its recommendations at the national level.

The methodology involves the systematic analysis of the literature dedicated to the efficacy and tolerability of pharmacological and psychosocial treatment methods in the case of patients with SUDs.

Monitoring will be done through periodic reassessments of the level of recommendations for each diagnosis, corresponding to epidemiological data at the national level and data from pharmaco-clinical research at the international level.

Table 2 presents the grading of recommendations formulated in the previous chapters, and specific observations have been mentioned whenever possible.

Table 2: Grading the recommendations for the prevention and treatment of SUDs

Recommendation	GRADE	Observations
1.1. Psychoeducational interventions	A	Such interventions should target not only vulnerable populations but also caregivers and other personnel involved in the healthcare/education of vulnerable groups
2.1. Secondary prevention	B	A comprehensive bio-psycho-social approach is strongly recommended
2.2. Guidelines for good practices in drug use prevention	C	Although there are multiple guidelines available worldwide, it was not demonstrated that guideline-focused interventions were significantly superior to other interventions

3.1. Training of specialists in the field of addiction therapy	B	All mental health specialists involved in the healthcare of patients with SUD should participate in such training
3.2. Intensification of harm-reduction interventions	C	The long-term efficiency of this intervention is still to be demonstrated
3.3. Enhancing the healthcare system's capacity for ensuring adequate detox treatment	B	National policy focused on funding and developing hospital resources for this intervention is needed
3.4. Post-detox treatment	B	Same observation as above
3.5. Reducing patient access to DOAs	B	National policies in this domain are needed
3.6. The need for a treatment guideline for patients diagnosed with SUDs	C	The guideline-focused interventions still need to be proven superior to other interventions

DISCUSSIONS

The recommendations formulated in the present paper may be considered a first draft for a framework that integrates multiple components to assist patients with SUDs. Although several therapeutic guidelines and good practices have been explored here, their recommendations and observations cannot be extrapolated to any country due to specific, regional aspects regarding the peculiarities of drug use, demographic data, local laws and healthcare policies, etc. This is an argument for constructing a more comprehensive national policy for the prevention of DOA use and treatment of individuals with SUDs through extending the Romanian "National Drug Strategy 2022-2026" [1] by adding more practical recommendations. The main directions of development in the domain of assisting vulnerable individuals to DOA use refer to psychoeducational measures in the general population, training professionals from different categories (professors, educators, psychologists, social workers, psychiatrists, GPs, etc.), promoting de-stigmatization and fighting against self-stigmatization, ensuring adequate protocols and funding for detoxification and post-detoxification protocols, and formulating general therapeutic recommendations and good practices for patients with SUDs.

This paper's limitations refer to the fact that only two authors scored the level of strength for each recommendation and to the paucity of available data regarding certain aspects of the DOAs' use in Romania, which reduces the ability to formulate clear, evidence-based recommendations on certain topics. Also, this was not a systematic review, so important primary and secondary reports may have been missed. Therefore, as a direction for further research, a comprehensive systematic literature review is expected to consolidate evidence-based recommendations for the prevention and treatment of patients with SUDs and to foster national policies in the domain of fighting against drug addictions.

CONCLUSION

Prophylaxis of DOA use in vulnerable populations, secondary prophylaxis and treatment in patients with SUDs, and educational measures for specialists who are involved in the healthcare of such patients are the pillars of a national policy dedicated to reducing the prevalence of SUDs and this pathology's negative social, psychological, economic and medical consequences. In order to attain this purpose, multidisciplinary teams are needed to explore different components of the extremely complex phenomenon that is SUD, and to find the most appropriate measures to counter the risk factors and to enhance resilience traits. The anti-drug use policies should target all populational groups, starting from children of school age exposed to the use of NPAs, psychostimulants, or cannabis, to active adult individuals who may become dependent on virtually any DOAs, or patients with psychiatric disorders who may abuse their prescribed medications or might combine them with DOAs, and up to the elderly population who may abuse analgesics or sedatives.

Conflicts of interest and sources of funding

The authors declare no conflict of interest. No artificial intelligence automatically generated text was inserted in this manuscript, and no image was previously published in another journal or is under consideration of being published elsewhere.

Authors' contribution

Conceptualization, O.V., V.A.V; methodology, V.A.V., O.V.; software, O.V.; validation, O.V.; formal analysis, V.A.V., O.V.; investigation, V.A.V., O.V.; resources, O.V., V.A.V.; data curation, O.V.; writing—original draft preparation, O.V., V.A.V.; writing—review and editing, V.A.V., O.V.; visualization, O.V.; supervision, V.A.V., O.V.; project administration, V.A.V., O.V. Both authors have read and agreed to the published version of the manuscript.

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